Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

With respect to the signed and initialed copy of the information disclosure statement received from the U.S. Patent and Trademark Office ("PTO"), applicants note that the listing to reference 33 was crossed out. The complete citation for the reference is:

> Peters et al., "The Biology of Tospoviruses" *In: Pathogenesis and Host Specificity in Plant Diseases*, vol III, Viruses and viroids. R.P. Singh, U.S. Singh and K. Kohmoto (Eds.), Pergamon Press (1995).

In view of the fact that the PTO has already considered the reference, applicants respectfully request that the PTO provide a form PTO 892 listing the reference with the next office action.

The objections to claims 5 and 9 have been overcome by the above amendments and should therefore be withdrawn.

The rejection of claims 4-9 under the judicially-created doctrine of obviousness-type double patenting over claims 2-6 and 8-22 of U.S. Patent No. 6,329,568 to Gonsalves et al. ("Gonsalves") is respectfully traversed.

Claim 2 of Gonsalves relates to a *Tospovirus* resistant plant that includes "a transgene inserted into its genome, said transgene expressing either a translatable or nontranslatable mRNA coding for a nucleocapsid polypeptide fragment which is at least about half the length of a full length nucleocapsid protein of a *Tospovirus*...."

Claim 3 of Gonsalves relates to a method for providing a host plant with resistance to infection by a *Tospovirus* that includes the step of "inserting a transgene into the host plant, said transgene expressing either a translatable or nontranslatable mRNA coding for a nucleocapsid polypeptide fragment which is at least about half the length of a full length nucleocapsid protein of a *Tospovirus*...." Claims 4-6 of Gonsalves depend from claim 3 and recite specific nucleotide sequences.

Claim 8 of Gonsalves relates to a DNA construct that includes, in addition to promoter and termination sequences, "a DNA molecule encoding either a translatable or nontranslatable mRNA coding for a less than full length nucleocapsid polypeptide fragment which is at least about half the length of a full length nucleocapsid protein of a *Tospovirus*...." Claims 9-22 ultimately depend from claim 8.

The PTO has taken the position at page 4 of the outstanding office action that the presently claimed invention is not patentably distinct over the above-identified claims of Gonsalves. Applicants respectfully disagree. None of claims 2 , 3, and 8 of Gonsalves nor any of claims 4-6 and 9-22 of Gonsalves specify an isolated DNA construct that includes a "DNA molecule ... capable of transcription to a nontranslatable messenger RNA that does not translate to a nucleocapsid protein of an L serogroup *Tospovirus* wherein, when the DNA construct is transformed into a plant cell, the DNA molecule is transcribed into the nontranslatable messenger RNA which exists at low level density readings of 15-50 as measured using a scanner and image analysis program. Because the invention claimed in Gonsalves fails to teach or suggest all of the above-identified limitations of claim 4, the obviousness-type double patenting rejection of claims 4-9 is improper.

The PTO's assertion is that the claims of Gonsalves do not state that the presently claimed embodiment is excluded and, therefore, these claims encompass the presently claimed embodiment. This position is improper in several respects. Firstly, even if the claims of Gonsalves entirely encompass the claimed invention (which they do not), it is not true that a genus necessarily renders a species unpatentable. The PTO bears the burden of demonstrating why the referenced genus would have rendered a claimed species obvious. Aside from indicating the above relationship (which in any event is inaccurate), the PTO has failed to satisfy its burden. Secondly, the invention claimed in Gonsalves (i) contains limitations not present in the presently claimed invention, and more importantly (ii) fails to teach or suggest certain limitations that are present in the presently claimed invention. In particular, the presently claimed DNA construct is not limited to those that encode translatable or untranslatable RNA encoding a less than full length nucleocapsid fragment, but it is limited to those that upon transformation into a plant cell are transcribed into nontranslatable messenger RNA which exists at low level density readings of 15-50 as measured using a scanner and image analysis program. Nowhere do the claims of Gonsalves teach or suggest the latter limitation.

For these reasons, the rejection of claims 4-9 under the judicially-created doctrine of obviousness-type double patenting over claims 2-6 and 8-22 of Gonsalves is improper and should be withdrawn.

The rejection of claims 4-9 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claim 4-9 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The PTO appears to have asserted two bases for this rejection.

As a first basis, at page 8 of the outstanding office action, the PTO suggests that written description is provided only for those constructs encoding nontranslatable half-length transcripts, but not any other constructs. As noted below, however, the results presented in the present application demonstrate to one of ordinary skill in the art that resistance to closely related *Tospoviruses* can be achieved with both nontranslatable full length and half-length transcripts when the transcripts are expressed at low levels in the transformed plants/plant cells.

The present application contains details concerning a number of experiments performed by the inventors. Having previously demonstrated (in this same application) the relationship between transgenic plants expressing high levels of the nucleocapsid protein and resistance against more distantly related *Tospoviruses* (i.e., from a different serogroup), as well as plants expressing low levels of the nucleocapsid protein and resistance against closely related *Tospoviruses* (i.e., belonging to the same serogroup), the inventors conducted a series of experiments that demonstrated role of RNA-mediated resistance to closely related *Tospoviruses*.

In one experiment, the inventors prepared and tested transgenic plants that produced either the sense or the antisense N gene transcript (from isolate TSWV-BL) but not the nucleocapsid protein. The transgenic plants were then challenged with TSWV-BL. To produce these transgenic lines, DNA constructs were prepared to express the sense or antisense transcripts. These constructs are schematically represented in Figure 7 as mN and asN, and the preparation of plasmids pBI525-mN and pBI525-asN are described on page 45, line 26 to page 47, line 14. The results of this experiment, presented at page 48, lines 6-35, demonstrate that both the sense transcripts and antisense transcripts, when expressed at low levels, afforded resistance. The transgenic plant lines expressing the sense transcripts (designated mN in the table on page 48) contain the construct mN described above, and lines expressing the antisense transcripts (designated asN in the table on page 48) contain the construct asN described above.

In a subsequent test of the same transgenic plant lines, four mN plant lines and three asN plant lines with either high or low levels were selected and challenged with closely related and more distantly related *Tospoviruses*. The results of this experiment are reported

and discussed on page 50 to page 53, line 9. In particular, those mN or asN lines expressing low levels of the RNA transcript showed resistance to both the TSWV-BL *Tospovirus* isolate whose N gene was used to prepare the respective constructs as well as closely related isolates (e.g., TSWV-10W). In further testing the mechanism of action using protoplasts derived from the low or high expressing mN lines, it was demonstrated that the high expressing lines permitted viral replication but the low expressing lines did not (page 51, line 27 to page 52, line 9).

In a second experiment, the inventors prepared and tested transgenic plants that produced either the sense or the antisense half-N gene transcript (from isolate TSWV-BL), the transcripts being in either translatable or nontranslatable form. The transgenic plants were then challenged with TSWV-BL. The production of translatable and nontranslatable constructs and plasmids containing them is described at page 53, line 27 to page 55, line 6. The nontranslatable constructs are schematically represented in Figure 8 as 1N′ (nontranslated first half) or 2N′ (nontranslated second half), and the corresponding plasmids are designated as pBI525-1N′ and pBI525-2N′, respectively. The results of this experiment, which are reported and discussed at page 56, line 17 to page 57, line 23, demonstrate that both the nontranslated sense half-transcripts and nontranslated antisense half-transcripts afforded resistance.

Thus, these experiments taken together teach that RNA-mediated protection using nontranslatable transcripts, whether full length or about half length, affords resistance to closely related *Tospoviruses* (i.e., those belonging to the same serogroup). Because the experimental work was conducted with TSWV-BL DNA, and TSWV-BL is an L serogroup *Tospovirus*, the results clearly support the use of such DNA constructs to provide RNA mediated resistance to L serogroup *Tospoviruses*.

As a second basis, at page 8 of the outstanding office action, the PTO suggests that the specification does not correlate any function with the nontranslatable mRNA other than the function of conferring to plants resistance against L serotype *Tospoviruses*. In citing *Fiers v. Revel v. Sugano*, 984 F.2d 1164, 25 USPQ 2d 1601 (Fed. Cir. 1993), the PTO appears to suggest that a specific nucleotide sequence is required. Applicant submits that the demonstration of affording resistance is all that is necessary in this instance and that the recitation of a specific nucleotide sequence is not required by *Fiers*.

In *Fiers*, the Federal Circuit found that conception of a DNA molecule, a product, required disclosure of the structure of that product and not a simply a method for

obtaining the product. 984 F.2d at 1169. The relevant disclosures by the parties Fiers and Revel failed to describe the claimed product, the DNA molecule, by any complete nucleotide sequence. *Id.* at 1167. The relevant disclosure by the party Sugano, on the other hand, did describe the claimed product via the complete nucleotide sequence. *Id.* Importantly, the Federal Circuit found that the disclosure of the correct and complete DNA sequence by Sugano satisfied the written description requirement for "DNA coding for B-IF," which does not recite the sequence *per se*. *Id.* at 1172.

The presently claimed invention concerns a DNA construct and its method of use. With respect to the claimed DNA construct, the present application identifies the DNA sequence for the nucleocapsid protein of a TSWV L serogroup isolate (e.g., TSWV-BL) and specific modification(s) made to the DNA sequence so that it affords a nontranslatable transcript (see above description for the production of plasmids containing the constructs). Moreover, as noted above, applicants demonstrated that RNA-mediated resistance could be achieved with low expression levels of nontranslatable transcripts, *regardless* of the exact structure of those transcripts (i.e., using full length transcripts as well as two approximately half-length transcripts). Thus, the presently claimed invention is entirely consistent with *Fiers* given that the disclosure of the present application does define how to make and use the DNA construct, including the relevant sequences and the modifications to those sequences.

For these reasons, the rejections of claims 4-9 for lack of written descriptive support is improper and should be withdrawn.

The rejection of claims 4-9 under 35 U.S.C. § 112 (first paragraph) as being non-enabled is respectfully traversed.

The basis asserted at page 10 of the outstanding office action is that the present application fails to teach other methods of preparing DNA molecules encoding nontranslatable mRNA, which DNA molecules can be used to impart resistance to L serogroup *Tospoviruses*. Applicant submits that one of ordinary skill in the art could achieve the desired result using any of a variety of recombinant techniques. As noted by the PTO, applicants used the insertion of a frameshift mutation and several stop codons as illustrated in Figures 7 and 8. However, as evidenced by U.S. Patent No. 5,583,021 to Dougherty et al. ("Dougherty") (copy attached hereto as Exhibit 1), the various techniques available to those of ordinary skill in the art include: insertion of a complete stop codon (*see* Dougherty at col. 7, lines 23-24 and 26-48); mutation of an existing codon to convert it to a stop codon (*see* Dougherty at col. 7, lines 24-25 and 49-60); insertion of one or more nucleotides (but not

complete codons) to induce a frameshift that affords a premature stop codon (*see* Dougherty at col. 7, line 61 to col. 8, line 9); combinations of the above approaches to induce multiple stop codons (*see* Dougherty at col. 8, lines 10-20); or removal of the start codon either with or without introduction of stop codons (*see* Dougherty at col. 8, lines 29-36). Dougherty indicates that the techniques for achieving these mutations are fully disclosed in known and available laboratory manuals (*see* Dougherty at col. 8, lines 37-42).

Thus, although applicants utilized one such approach for inducing the transcription on a nontranslatable mRNA, one of ordinary skill in the art would understand that other approaches can likewise achieve the same results. For this reason, the rejection of claims 4-9 for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: December 17, 2003

Edwin V. Merkel
Registration No. 40,087

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1128
Facsimile: (585) 263-1600

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☒ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Mail Stop _____, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450

☐ transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) _____.

12/17/03
Date

Signature

Jane C. Wirszyla
Type or Print Name